UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

08/949,904

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT		ATTY. DOCKET NO.
08/949,904	10/15/97	LAVALLIE	E	GI-5288B

EXAMINER

HM21/0819

STEVEN R LAZAR
GENETICS INSTITUTE INC
87 CAMBRIDGE PARK DR
CAMBRIDGE MA 02140

UNGAR, S

ART UNIT	PAPER NUMBER
1642	7

DATE MAILED: 08/19/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 7/8/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 (month(s)), or ~~thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-27 is/are pending in the application.
Of the above, claim(s) 1-17, 21, 24, 26 + 27 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 18-20, 22, 23 + 25 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 1 1/2
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

* U.S. GPO: 1998-404-496/40517

1. The Election filed May 18, 1998 (Paper No. 5) the Supplementary Amendment filed July 7, 1998 (Paper No. 6) and the Election filed August 6, 1998 (Paper No. 7) in response to the Office Action mailed April 29, 1998 (Paper No. 4) are acknowledged and have been entered. Claims 1-27 are pending in the application and Claims 1-17, 21, 24 and 26-27 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 18-20, 22, 23 and 25 are currently under prosecution.

2. Applicant's election with traverse of Group IV, claims 18-20, 22, 23 and 25 in Paper No 6 is acknowledged. The traversal is on the ground(s) that (a) search of inventions I-III would not impose a serious burden on the examiner, (b) the inventions of Groups I-III have not been shown to be distinct, © the claims of Groups IV and VI-VII have not been shown to be distinct. The arguments have been noted but have not been found persuasive because (a) the literature search, particularly relevant in this art, is not coextensive and different searches and issues are involved in the examination of each group and (b and c) MPEP 802.01 provides that restriction is proper between inventions which are distinct and goes on to define distinct as two or more subjects that are related but capable of separate manufacture, use or sale as claimed, thus for the reasons disclosed in Paper No. 4, the inventions are clearly distinct. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise,

and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

4. The specification is objected to under 35 USC 112, first paragraph, and Claim 20 is rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to use a composition comprising a therapeutic amount of at least one human SDF-5 polypeptide.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

The claims are drawn to a composition comprising a therapeutic amount of at least one human SDF-5 polypeptide. This includes therapeutic use of the composition for a plethora of diseases or conditions. The specification teaches inducing the formation or maintenance of cartilaginous tissue in a patient comprising administering an effective amount of a composition comprising SDF-5 protein (p. 3, lines 30-35) and further teaches that the compositions may be further used in methods for treating a number of tissue defects and healing and maintenance of various types of tissues and wounds (p. 7, lines 32 - page 8 line 15) and further teach that the therapeutic compositions are valuable for veterinary applications, particularly for domestic animals and thoroughbred horses in addition to humans (p. 21, lines 29-35) and further teach methods of administration of the therapeutic composition (p. 22, lines 5-24) and that the dosage regimen will be determined by the attending physician (p. 22, lines 25-34) and that the protein may be used to treat

autoimmune diseases and to stimulate or suppress the immune system (p. 26 line 10-30 line 23). One cannot extrapolate the teaching of the specification to the scope of the claims because the specification does not set forth sufficient teachings to allow one skilled in the art to use the claimed composition therapeutically. The specification does not provide teachings to establish effective dosages other than to suggest that the physician should establish the dosage regimen. The specification as written appears to be an invitation to experiment. Applicant's attention is directed to Brenner v. Manson, 383, U.S. 519, 148 USPQ 689 wherein the court held that "a patent is not a hunting license". Applicant discloses *in vitro*, cell culture experiments to support the use of the therapeutic composition. However, *in vitro* assays cannot duplicate the complex conditions of *in vivo* therapeutic use of a composition. In the assays, the therapeutic agent is in contact with cells during the entire exposure period. This is not the case *in vivo*, where exposure to the target site may be delayed or inadequate. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The therapeutic composition may be inactivated *in vivo* before producing a sufficient effect, for example, by proteolytic degradation, immunological activation or due to an inherently short half life of the protein and the *in vitro* tests of record do not sufficiently duplicate the conditions which occur *in vivo*. In addition, the therapeutic composition may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the therapeutic composition has no effect, circulation into the target area may be insufficient to carry the therapeutic composition and a large enough local concentration may not be established. The

specification provides insufficient guidance with regard to theses issues and provides no working examples which would provide sufficient guidance to one skilled in the art to practice the invention which would allow one of skill in the art to predict the efficacy of the claimed therapeutic composition with a reasonable expectation of success. For the above reasons, one of skill in the art would be forced into undue experimentation in order to practice the claimed invention.

5. Claims 18 and 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is indefinite in the recitation of the phrase "comprising an amino acid sequence according to SEQ ID NO:". The claim is indefinite because it is not clear whether the phrase "according to" is open or closed and whether it encompasses the entire sequence of SEQ ID NO: 2 or 3 or simply selected sequences from those sequences.

Claim 20 is confusing because it claims "a composition comprising a therapeutic amount of at least one human SDF-5 polypeptide according to claim 19". The claim is confusing because claim 19 only recites one human SDF-5 polypeptide which is the amino acid sequence from amino acid 21 to amino acid 295 of SEQ ID NO:2.

Double Patenting

6. Claims 18-20, 22, 23 and 25 provisionally rejected under the judicially created doctrine of double patenting over claims 18-20, 22, 23 and 25 of copending Application No. 08/848,439. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming identical subject matter.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. In re Schneller, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 18, 23 and 25 are rejected under 35 U.S.C. § 102(a) as being anticipated by Shirozu et al (Genomics, 1996, 37:273-280).

The claims are drawn to a purified SDF-5 polypeptide comprising an amino acid sequence according to SEQ ID NO:3, wherein the protein has a molecular weight of about 30-35 kd and the ability to regulate the transcription of one or more genes.

Shirozu et al teach an SDF-5 protein with 100% sequence identity to SEQ ID NO: 3 (see Fig 2, page 276 and Sequence Search Printout, US-08-848-439-2.rspt, Result No. 3, attached). Because the structure of the prior art polypeptide is

identical to the claimed polypeptide, the molecular weight and the functions recited would be inherent properties of the prior art polypeptide.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

10. Claims 18, 19, 20 and 22 are rejected under 35 U.S.C. § 103 as being unpatentable over Shirozu et al (Genomics, 1996, 37:273-280).

It is noted that claim 20 claims the SDFf-5 polypeptide in a therapeutic

amount, however, this limitation is viewed as a recitation of intended use and therefore is not given weight in comparing the claim with the prior art. Claim 21 reads on the ingredient *per se*, which is SDF-5 polypeptide according to claim 19.

The claims are drawn to a purified SDF-5 polypeptide comprising an amino acid sequence according to SEQ ID NO: 2, a method of producing the protein comprising culturing a DNA molecule comprising the nucleotide sequence o SEQ ID NO:1, nucleotides #316-#1143 and recovering and purifying a protein comprising the amino acid sequence of amino acid #21-#295 as shown in SEQ ID NO:2, a composition comprising a therapeutic amount of SDF-5 polypeptide.

Shirozu et al teach as set forth above and a cDNA molecule (see Abstract and Table 2, page 275) that encodes an SDF-5 protein sequence that is 97.6% identical to 97.8% of SEQ ID NO:2. Shirozu et al do not teach a sequence identical to SEQ ID NO:2 but rather teach a sequence with two conservative amino acid substitutions at amino acids 3 and 6 and two nonconservative amino acid substitutions at amino acids 2 and 12 and do not teach a method of producing the protein as disclosed in the instant application.

The specification teaches on page 5 that the human SDF-5 protein exists as a heterogeneous population of active species with varying N-termini and that the first 17 to 24 amino acids appear to be involved in signally for the secretion of the mature peptide and that it is expected that active species may optionally include the signal peptide. The claimed polypeptide is *prima facie* obvious over the prior art polypeptide because it differs in only amino acids 2, 3, 6 and 12. These minor changes in chemical configuration or design of the molecule discovered or made by applicants over the prior art are considered to be de minimus since there is no

evidence that these positions are essential for the biological activity of the mature protein that is produced which comprises amino acids 21-295 of SEQ ID NO:2. See Ex parte Anderson 30 USPQ2d 1994 (PTO Bd. Pat. App. & Int.). In the absence of evidence to the contrary, the burden is upon the applicant to prove that the polypeptides produced would be functionally different than produced using conventional methods and to establish patentable differences. Further, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express the cDNA taught by Shirozu et al by culturing a cell transformed with the DNA molecule of Shirozu and isolating and purifying the polypeptide expressed. One of ordinary skill in the art would have been motivated to produce the polypeptide in order to further characterize the function of the polypeptide.

11. No claims allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731. The fax phone number for this Art Unit is (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 USC 132 or which otherwise require a signature may be used by the applicant and should be addressed to lila.feisee@uspto.gov.

All internet e-mail communications will be made of record in the application

file. **PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of USC 122.** This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
August 10, 1998

LILA FEISEE
SUPERVISORY PATENT EXAMINER